interval each knee received a series of 5 weekly intra-articular hyaluronic acid injections every six months. During that same interval the patient wore CAB on each knee when he went to bed - ie. approximately 7 hrs. nightly. Again during this period both symptomatic and functional benefit were noted. After this period, commercial difficulty was encountered in obtaining replacement electrodes and appropriate gel and the brace could no longer be worn. Again symptomatic and functional changes were noted.

Results: At the onset, functionally the patient was barely able to walk from my office to his car in the parking lot (ie. approx. 30 yds.) with a cane. Pain was 10/10. Using only serial intra - articular HA injections resulted in only minimal pain reduction - ie. 8/10. His functional ability to walk remained at approx. 30 yds. However after adopting concomitant combination therapy of both modalities the patient was aware of a progressive gradual reduction in his bilateral knee pain after 3 months. After 9 months his pain was 0/10 and he was able to walk >60 yds. Of interest the functional and symptomatic benefit was gradually diminished once he no longer had access to the necessary replacement electrodes and gel ie. 8/10. His ability to walk was decreased to approx. 60 yds. He continues with intra-articular HA injections to both knees every six months - both symptomatic and functional parameters have not significantly changed.

Conclusions: Although this is a single case, it has clinical importance. That the CAB was therapeutically valid is underlined by the fact that it was FDA approved for both osteoarthritis of the knee and rheumatoid arthritis of the hand. Given its demonstrated clinical efficacy, it is known that prototypes were being developed for other joints in the body as well as an improved version of the brace itself. The clinical significance of concomitant combination HA injection and CAB therapy needs to be validated. In the past it has been possible to grow a patient's cartilage outside the joint - ie. in a Petri dish. The inevitable difficulty however was to get cartilage to effectively attach to subchondral bone. This process may offer a solution to this dilemma and merits ulterior independent investigation.

Therapy – Non-Pharmacologic

508

APPLICABILITY AND USEFULNESS OF "CONDITIONED" CHONDROCYTES IN THREE-DIMENSIONAL IN VITRO ARTHRITIS MODELS

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Purpose: To evaluate the expediency of an inflammation-sensitive and disease-regulated cyclooxygenase-2 (Cox-2) promoter to exploit therapeutic potential of canine interleukin (IL)-4 gene in vitro.

Methods: Chondrocytes from canine knee cartilage were "conditioned" by ex vivo gene transfer using IL-4 as a therapeutic transgene downstream of Cox-2 promoter (devoid of viral sequence). Chondrocyte/scaffold constructs were engineered using two types of biomaterials. The cells were either encapsulated in alginate microspheres or trapped in transplants. The latter were generated by employing a rat-tail collagen type I cartilage regeneration system. Recombinant proinflammatory canine cytokines IL-1β and tumour necrosis factor (TNF)α were used to simulate inflammatory arthritis in chondrocytes within these scaffolds. Multiple inflammation and cartilage markers were monitored to evaluate the antiinflammatory and regulatory characteristics of IL-4.

Results: It was shown that in the presence of proinflammatory cytokines, IL-1β and TNFα, the Cox-2 promoter was "switched on" to drive the expression of antiinflammatory IL-4 gene. The controlled and fine-tuned expression of IL-4 down-regulated the inflammatory cytokines such as IL-1β, IL-6, TNFα and enzyme mediators as inducible nitric oxide synthase (iNOS), Cox-2 and matrix metalloproteinases (MMPs)-3 and -13. Synthesis of two major destructive mediators namely nitric oxide (NO) and prostaglandin E2 (PGE2) was also reduced. At the same time, an up-regulated expression of the insulin-like growth factor (IGF)-1, IL-1 receptor antagonist (IL-1Ra) and collagen type II was observed. These findings represent proof-of-concept of our previous studies in monolayer cultures. There was virtually no marked difference between the two scaffolds in the context of expression pattern of various marker genes. However, it is tempting to speculate that alginates are easy to use and can enter in small cartilage defects but could be fragile during surgery. On the other hand, the collagen scaffold may be useful to cover larger cartilage lesions. While these results substantiate our previous findings, at the same time they potentiate the need for application of a disease-driven, self-limiting, species-specific therapy for osteoarthritis in vivo.

Conclusions: We propose that the application of cytokine therapy based on ex vivo gene transfer through a non-viral, disease-regulated promoter combined with autologous chondrocyte transplantation could potentially serve as a useful tissue engineering tool towards devising therapeutic strategies for the treatment of osteoarthritis.

509

HIP JOINT LAVAGE IN OSTEOARTHRITIS: ITS SAFETY AND EFFICACY. EXPERIENCE IN AN OUTPATIENT CARE DEPARTMENT

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Purpose: Among the rheumatic diseases, osteoarthritis (OA) is the most frequent. Joint lavage is just another way to treat it. It is useful in degenerative and inflammatory diseases. It has been used either in knee and shoulder joints, and it is getting more used as an effectiveness treatment in hip joint. The aim of the hip joint lavage (HJL) is to evacuate fibrin remains and microcrystal, dissolve inflammatory molecules, and, also, induce vasoconstriction through cooling. It is done in a specific box in our outpatient clinics care office. The objective of this study is to evaluate the efficacy and the safety of the HJL after one and three months, in patients affected of OA of the hip.

Methods: We recruited 22 patients (22 hips), mean age 70 years-old, with painful hip OA grades II and III (Kellgren-Lawrence Index), from our outpatient clinics, in Hospital de la Santa Creu I Sant Pau, in Barcelona. We used the Golding technique for the punction, to access the joint, with a 1.1 mm diameter trochar, and using local anesthesy with Mepivacaine 2%. We also performed a 500 cc physiological serums 0.09% perfusion (at 18-20°C) by positive pressure. We also performed a second punction to allow the way out of the serum. The whole intervention took 30 minutes. The efficacy was evaluated by WOMAC, LEQUESNE and Pain-VAS indexes. Statistical analysis was completed by SPSS program.

Results: HJL showed efficacy diminishing Pain-VAS mean from basal register to 3-months one (7.33 to 5.33), which represented a significant difference ($p<0,001$). WOMAC pain domain improved at 3 months, without significant differences, though. The other parameters evaluated are shown separately in the following table, with significant differences between basal and later registers (p=NS).

There were no serious adverse events. Two mild complications were seen: local pain during the intervention in one patient, and vagal syndrome in another one. All of them were recovered and we did not need to stop the intervention.

Table 1

	Mean
LEQUESNE basal	13,14
LEQUESNE month1	11,08
LEQUESNE month 2	11,00
WOMAC stiffness basal	125,00
WOMAC stiffness month 1	98,33
WOMAC stiffness month 2	90,83
WOMAC functional ability basal	975,36
WOMAC functional ability month 1	805,17
WOMAC functional ability month 2	841,67

Conclusions: The HJL shows efficacy and safety in patients with symptomatic hip OA. We can consider it as a low cost alternative treatment for OA. It is performed quickly, in 30 minutes, and there are not serious complications.

510

HIGH INTENSITY LASER THERAPY IN THE REGENERATION OF HUMAN CARTILAGE CHRONIC LESIONS

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Purpose: It is widely known that joint cartilage lesions have a very poor healing capacity. Many studies have explored cartilage regeneration using various techniques involving abrasion, drilling of sub-chondral bone, mosaic-plastic, periosteal and perichondral transplantation, tissue engineering and cell therapy (Autologous Chondrocyte Implantation (ACI) more recently mesenchimal cell one-step implant). With the aim to find a new approach to treat cartilage lesions, we investigated the effects of a High Intensity Laser Therapy (HILT) as a non-invasive method to stimulate tissue repair *in vivo*.
Methods: Human articular cartilage was obtained from the knees of 9 patients affected by chronic cartilage lesions of the femoral tibiae joint due to repeated sport-traumas. All patients were amateur soccer players referring pain during sport activity. The lesions were investigated by RMI and the patients were scheduled for Autologous Chondrocytes Implantation (ACI). The patients were divided into two groups: the first group (henceforth HILT group) (4 males/1 females, mean age: 32 yrs) was processed with Nd:YAG laser (3,000 Joule) daily, 15 times in the 3 weeks required to perform transplantation. 4 patients (henceforth control group) underwent to ACI protocol (3 males/1 female, mean age:31 yrs). When the healthy cartilage biopsy from unloaded zone was taken for chondrocyte isolation and expansion (T0), a small cartilaginous fragment was harvested from the pathologic area. Another specimen was taken just before cell implantation (T1) to verify the efficacy of the laser treatment in both groups. Histological, immunohistochemical and molecular biology analyses were carried out on cartilage samples. The study has been approved by Ethics and Scientific Committees of Rizzoli Orthopaedic Institute and specimens were taken with patients' written consent.
Results: In the Hilt group at T1, the macroscopic observation of the treated zones showed in general a progressive growth of a new tissue from the edges to the central area of the lesions. In contrast, in the control group the lesions were still evident or in some cases covered by a fibro-cartilaginous layer. Histological appearance of the articular cartilage performed by Safranin-O staining in HILT group at T1 displayed, in some cases, a hyaline-like tissue with a good proteoglycan content in particular near the sub-chondral bone. In contrast, low proteoglycans presence and hypocellularity were observed in the control group. Immunohistochemical analysis showed some clusters of collagen type II positive zones in the HILT group and a down-regulation of a series of inflammatory markers.
Conclusions: These preliminary data indicate that HILT treatment is able to facilitate cartilaginous tissue formation in patients with chronic traumatic lesions. The quality of the regenerated tissue is good as concern the extracellular structure, the expression of typical matrix markers even in presence of some fibrocartilaginous features. A reduction of some degenerative molecules testify the anti-inflammatory action of this therapeutical approach.
Therefore, these results advocate the use of HILT for further in vivo studies and could be in particular suggested for the treatment of early cartilage lesions in osteoarthritic patients.

511

THE EFFECT OF NEUROMUSCULAR ELECTRICAL STIMULATION ON MUSCLE FUNCTION & FUNCTIONAL PERFORMANCE IN INDIVIDUALS WITH MODERATE TO SEVERE KNEE OSTEOARTHRITIS

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Purpose: Weakness of the quadriceps femoris muscle (QFM) is associated with many of the disabling symptoms of knee osteoarthritis (OA) including pain and functional impairment. Neuromuscular electrical stimulation (NMES) is a treatment modality that improves the strength of the QF and prevents atrophy in patients with knee OA. The purpose of the study was to evaluate the efficacy of a home-based NMES training programme in restoring QFM strength and knee function in a cohort of adults ($<$ 55 yrs) with moderate to severe knee OA according to the Kellgren-Lawrence grading scale.
Methods: Individuals were randomly assigned to an NMES training (n=11) or control group (n=8). NMES was applied using a portable garment based stimulator (Kneehab II, Bio-Medical Research, Galway, Ireland) for 20 min/day, 5 d/wk at an intensity maximally induced for 6 weeks. Subjects were familiarised with the testing procedures one week prior to baseline assessments. QFM cross-sectional area (MRI) and self report outcomes (Western Ontario & McMaster Universities Osteoarthritis Index and Short Form-36 Quality of Life Questionnaire) were measured at baseline and week 6. Isokinetic strength, isometric strength and functional ability (timed chair rise, stair climb and 25m walk) were assessed at baseline during the intervention at week 3 and at week 6.
Results: Compared to baseline, QFM cross-sectional area increased 6% ($p<0.05$), and isometric strength at 60° knee flexion increased 7% ($p<0.05$) at week 6 in the NMES group. WOMAC score improved ($p<0.05$) in the NMES group. Performance in the chair rise, 25 m walk or stair-climb did not change in either group.
Conclusions: In adults $<$ 55 yrs with moderate to severe knee OA, NMES improves isometric knee extensor strength. Patients also reported a subjective benefit in response to a 6 week NMES program.